REMARKS

The present amendment is submitted in accordance with the Revised Amendment Format as set forth in the Notice provided on the USPTO web site for the Office of Patent Legal Administration; Pre-OG Notices; dated 1/31/03.

With the foregoing amendment, claims 1-15, 31 and 63 are pending in the application and presented for examination. Claims 5, 16-30, 32-62, and 64-66 have been canceled without prejudice or disclaimer. Claims 1 and 31 has been amended. Claims 67 is newly added. Support for the amendment to the claims and newly added claim is found throughout the specification as originally filed. More particularly, support for the amendment to claims 1 and 31 is found, *inter alia*, at page 6, lines 8-12, and page 7, lines 13-19 and 21-22 of the specification. Support for newly added claim 67 is found at page 60, lines 12-19 of the specification. No new matter has been introduced with the foregoing amendment. Reconsideration is respectfully requested.

The Invention

The present invention relates to nucleic acids and polypeptides for IRAK-4, a member of the IRAK family of protein kinases. Members of the IRAK family are indispensable signal transducers for members of the IL-1R/Toll family of transmembrane receptors, including IL-1 receptors, IL-18 receptors and LPS receptor.

Rejection Under 35 U.S.C. § 112, First Paragraph, Enablement

Claims 1-15, 31 and 63 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled. According to the Office Action, the specification does not enable a skilled person to make and use a nucleic acid which encodes a polypeptide which is 98% identical to SEQ ID NO: 1 or a nucleic acid encoding an amino acid which is a subsequence of a polypeptide which is 98% identical to SEQ ID NO: 2. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection. Applicants would like to respectfully point out that claim 4 recites a polypeptide comprising an amino acid sequence of SEQ ID

NO:1. In addition, claim 10 recites a nucleic acid comprising a nucleotide sequence of SEQ ID NO:2. As such, Applicants believe that claims 4 and 10 contain allowable subject matter.

The present invention provides nucleic acids and polypeptides for IRAK-4. Claim 1 has been amended to indicate that the claimed nucleic acid encodes a polypeptide having IL-1R/Toll family member signal transduction activity. As amended, claim 1 recites the following:

> 1. An isolated nucleic acid encoding an IRAK-4 polypeptide, said polypeptide having ***IL-1R/Toll family member signal transduction activity*** and at least about 98% amino acid sequence identity to SEQ ID NO:1 or to a subsequence thereof, wherein the amino acid sequence of the polypeptide comprises an alanine residue at an amino acid position corresponding to amino acid position 81 of SEQ ID NO:1, and wherein said nucleic acid comprises at least about 400 nucleotides.

In the Office Action, the Examiner has provided an example of a single amino acid substitution which causes a change in the protein's function (*see,* page 3 of the Office Action). In this example, a Glu to Val substitution in the beta subunit of hemoglobin causes a structural change in the protein such that its function is altered. In contrast to this example, however, the presently amended claims do not seek to encompass proteins lacking IRAK-4 function. As amended, claim 1 specifies that the claimed nucleic acid encodes a polypeptide that can transduce signals from IL-1R/Toll family members. It has been shown that IRAK-4 transduces signals from IL-1R/Toll family members *(see*, page 6, lines 8-12, and page 7, lines 13-19 and 21-22 of the specification). Using a luciferase reporter system, it was shown that transient overexpression of IRAK-4 leads to the activation of NF-κB, an indicator of IL-1R/Toll signal transduction by IRAK-4. As amended, the claimed nucleic acid encodes a polypeptide which retains a characteristic of IRAK-4, namely IL-1R/Toll family member signal transduction activity. Claim 31 has been amended in a similar manner as claim 1.

IL-1R/Toll family member signal transduction activity is easily tested using a luciferase assay system or other means known to one of skill in the art (*see*, 60, lines 13-19 of the specification). Furthermore, as discussed in the following section in response to the Written Description rejection, the specification provides ample guidance for the identification of the claimed members. As such, Applicants respectfully request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejection Under 35 U.S.C. § 112, First Paragraph, Written Description

Claims 1-15, 31 and 63 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. According to the Office Action, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. To the extent the rejection is applicable to the amended set of claims, Applicants respectfully traverse the rejection.

Claims 1 and 31 have been amended to clarify that the claimed nucleic acid encodes a polypeptide that can transduce signals from IL-1R/Toll family members. As such, the present invention clearly defines the claimed polypeptide as one having IRAK-4 activity, namely, the ability to transduce signals from IL-1R/Toll family members. Based on the information in the specification, one of skill in the art would be able to recognize polypeptides which have IL-1R/Toll family member signal transduction activity and at least about 98% amino acid sequence identity to SEQ ID NO:1. The specification provides ample guidance regarding the identification of the claimed members (*see*, page 26, lines 28-32, and pages 27 and 28 of the specification). For example, the specification teaches the use of stringent hybridization conditions and screening libraries to identify polymorphic variants, alleles, and interspecies homologs that are substantially identical to an IRAK-4 gene. In addition, Claims 2, 3, 7, 8 and 9 teach specific members of the genus and indicate the amino acid changes in the sequence. NF-κB activation, an indicator of IL-1R/Toll signal transduction by IRAK-4, is easily tested using a luciferase assay system or other means known to one of skill in the art (*see*,

page 60 of the specification). Since IL-1R/Toll family member signal transduction activity is a common attribute which identifies members of the genus, and this property is recited in the claims, Applicants respectfully request that the rejection be withdrawn.

Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 12 has been rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite. According to the Office Action, the term "specifically" is a conditional term and renders the claim indefinite. Applicants respectfully traverse the rejection.

Claim 12 recites the following:

> 12. The nucleic acid of claim 1, wherein the polypeptide specifically binds to antibodies generated against a polypeptide comprising an amino acid sequence of SEQ ID NO:1.

According to the specification,

> "Antibody" refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that ***specifically*** binds and recognizes and antigen. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. (*See*, page 33, lines 24-28 of the specification.)

It is well-know to one of skill in the art that an innate property of antibodies is that they specifically recognize and bind antigens. The term "specifically" as used in the art means that the antibodies are specific for the antigens they can recognize and bind; they cannot bind antigens that they do not recognize. Thus, they are specific. Furthermore, the specificity of the antibody binding is determined by the antigen the antibody is generated against. The antibodies of claim 12 are generated against polypeptides comprising an amino acid sequence of SEQ ID NO:1. Thus, the antibodies have specificity for a polypeptide comprising an amino acid sequence of SEQ

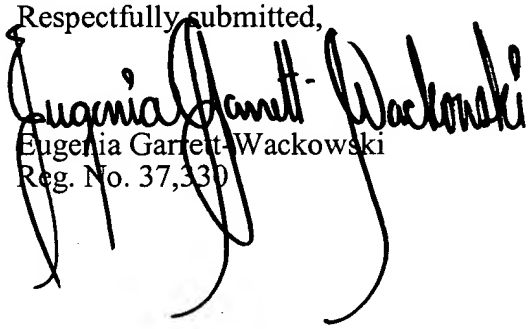
ID NO:1, and peptides which will bind to these antibodies will have a structure recognizable by the antibodies. Applicants respectfully request that the rejection be withdrawn.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 925-472-5000.

Respectfully submitted,



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